DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

NEW YORK DISTRICT
850 THIRD AVENUE
BROOKLYN, NY 11232
TEL. (718) 965-5300

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**WARNING LETTER**

**CERTIFIED MAIL**
**RETURN RECEIPT REQUESTED**

Daniel R. Martin
President and Chief Executive Officer
E-Z-EM, Inc.
717 Main Street
Westbury, New York 11590

December 3, 1996

Ref: 22-NYK-97

Dear Mr. Martin:

During an inspection of your manufacturing facility located in Westbury, New York conducted between the dates of October 18 and November 19, 1996 our investigator documented deviations from the Current Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Part 211) causing your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act, as follows:

1. Failure to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process materials and drug products.

A. The matrix approach used to validate barium sulfate products consisted of conducting validation testing on three batches of only one product of a matrix group. For example, validation data for the high density group of Therapex liquid barium sulfate suspension products fails to include any validation testing on batches of E-Z-AC and Liquid Polibar Plus. Also, these suspension products have differences in formulation and flow rates from the product, Liquid Polibar, selected for validation testing.

B. There is no validation report or documented validation of the processes for manufacturing liquid barium sulfate suspension at the Westbury, NY facility.

2. Failure to establish and test for appropriate specifications for lots of active ingredient barium sulfate used in the manufacture of liquid barium sulfate suspensions and barium sulfate for suspension. There is no established specification nor testing for particle size.

3. Failure to establish adequate quality control procedures to assure that any failure of a drug product to meet any of its specifications is fully and thoroughly investigated.

A. The SOP, Investigation and Retesting Procedure For Out of Specification Chemistry Results, specifies that original test results may be disregarded after statistical evaluation when categorized as "no assignable cause". The SOP does not include a protocol for sampling (same or different sample), and retesting (number of retests).

B. An investigation of Liquid Polibar, batches 1B8687, 1B8688, and 1B8689 consisted of multiple retesting of the batches resulting in passing and failing test results for assay and total solids. The investigation failed to include a documented review of the batch production records and the control records for the components of the batches.

C. There was no documented investigation into the failure of Liquid Polibar batches 3C9625 and 3C9626 to meet the specification for potassium sorbate assay.

The above identification of violations and the observations on the FDA-483 issued at the end of the inspection are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the Current Good Manufacturing Practice Regulations. Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These include seizure and/or injunction.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be sent to Compliance Branch, Food and Drug Administration, New York District, 850 Third Avenue, Brooklyn, NY 11232, Attention: Laurence D. Daurio, Compliance Officer.

Sincerely,

Alonza E. Cruse
Acting District Director